IRISH MEDICINES BOARD ACTS 1995 AND 2006

MEDICINAL PRODUCTS(CONTROL OF PLACING ON THE MARKET)REGULATIONS,2007

(S.I. No.540 of 2007)

PPA1328/117/001
Case No: 2064922

The Irish Medicines Board in exercise of the powers conferred on it by the above mentioned Regulations hereby grants to

B & S Healthcare

Unit 4, Bradfield Road, **Ruislip**, **Middlesex**, **HA4 0NU**, **United Kingdom**

an authorisation, subject to the provisions of the said Regulations, in respect of the product

Pepcid 20mg Film-coated Tablets

The particulars of which are set out in Part I and Part II of the attached Schedule. The authorisation is also subject to the general conditions as may be specified in the said Regulations as listed on the reverse of this document.

This authorisation, unless previously revoked, shall continue in force from **12/06/2009**.

Signed on behalf of the Irish Medicines Board this

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A person authorised in that behalf by the said Board.

Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Pepcid 20 mg Film-coated Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 20 mg of famotidine.
For a full list of excipients, see 6.1.

3 PHARMACEUTICAL FORM

Film-coated (Tablets).
Beige, film-coated, round-cornered square tablets, engraved 'MSD 963' on one side and plain on the other.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Duodenal ulcer.
Prevention of relapses of duodenal ulceration.
Benign gastric ulcer.
Hypersecretory conditions such as Zollinger Ellison syndrome.
Healing of oesophageal erosion or ulceration associated with gastro oesophageal reflux disease.
Symptomatic relief of gastro oesophageal reflux disease.
Prevention of relapse of symptoms and erosions or ulcerations associated with gastro oesophageal reflux disease.

4.2 Posology and method of administration

It is unnecessary to time the dose in relation to meals: bioavailability is not clinically affected by food in the stomach.
In all cases the clinical response of the patient should be taken into consideration.
In benign gastric and duodenal ulceration, the dose of 'Pepcid' is one 40 mg tablet at night.

Duodenal ulcer
The recommended initial dose is one 40 mg tablet of 'Pepcid' at night. Treatment should continue for four to eight weeks. In most patients, healing occurs on this regimen within four weeks. In those patients whose ulcers have not healed completely after four weeks, a further four week period of treatment is recommended.

Maintenance therapy: For preventing the recurrence of duodenal ulceration, the reduced dose of 20 mg of 'Pepcid' at night is recommended. This 20 mg maintenance dose has been continued effectively in clinical studies for 12 months.

Benign gastric ulcer
The recommended dose is one 40 mg tablet of 'Pepcid' at night. Treatment should continue for four to eight weeks unless endoscopy reveals earlier healing. Patients with a suspected gastric ulcer should have gastric carcinoma excluded (see section 4.4).

Zollinger Ellison syndrome
Patients without prior antisecretory therapy should be started on 20 mg of 'Pepcid' every six hours. Dosage should then be adjusted to individual response: doses up to 800 mg daily have been used up to one year without the development of significant adverse effects or tachyphylaxis. Patients who have been receiving another H2 antagonist may be switched directly to 'Pepcid' at a dose higher than that recommended for new cases.

This starting dose will depend on the severity of the condition and the last dose of H_2 antagonist previously used.

Gastro oesophageal reflux disease
For the treatment of oesophageal erosion or ulceration associated with gastro oesophageal reflux disease, the recommended dosage is 40 mg of famotidine twice daily, which may be given for six to twelve weeks.

The recommended dosage for the symptomatic relief of gastro oesophageal reflux disease is 20 mg of famotidine twice daily, which may be given for six to twelve weeks. Most patients experience improvement after two weeks.

Maintenance therapy: For the prevention of recurrence of symptoms and erosions or ulcerations associated with gastro oesophageal reflux disease, the recommended dosage is 20 mg of famotidine twice daily. As with all chronic therapy, patients should be kept under regular surveillance.

Use in the elderly: 'Pepcid' should be used with caution in elderly patients. The recommended dosage in most elderly patients is the same as in younger patients for all indications (see above). No change in the incidence or type of drug related side effects were seen in treated elderly patients.

Use in impaired renal function: Since 'Pepcid' is excreted primarily by the kidney, caution should be observed in patients with severe renal impairment.

The dose should be reduced to 20 mg nocte when creatinine clearance falls below 10 ml/min.
Currently, no clinical data are available regarding dosage recommendations for patients undergoing haemodialysis.

Paediatric use
The efficacy and safety of 'Pepcid' in children have not been established.

4.3 Contraindications

Hypersensitivity to any component of this product. Cross sensitivity in this class of compounds has been observed. Therefore 'Pepcid' should not be administered to patients with a history of hypersensitivity to other H2-receptor antagonists.

4.4 Special warnings and precautions for use

Gastric carcinoma
Before the initiation of therapy for any gastric ulceration, malignancy should be excluded by appropriate diagnostic techniques. Treatment with H2-receptor antagonists (including famotidine) can mask symptoms and allow transient healing of gastric ulcer associated with underlying cancer. The consequences of a potential delay in diagnosis should be kept in mind particularly in patients of middle age or over, or with new or recently changed dyspeptic symptoms.

Impaired renal function
Since 'Pepcid' is primarily excreted via the kidney, caution should be exercised when treating patients with severe renal impairment.

As with all chronic drug therapy, patients should be kept under regular surveillance and hepatic and renal function should be periodically reviewed.

Dosage reduction should be considered when creatinine clearance falls below 10 ml/min (see 'Posology and method of administration').

4.5 Interaction with other medicinal products and other forms of interaction

No clinically important drug interactions have been identified.
Studies in normal volunteers have demonstrated that famotidine does not interact with other compounds metabolised by the cytochrome P450 linked drug metabolising enzyme system. These include warfarin, theophylline, phenytoin, diazepam, propranolol, aminopyrine and phenazone. Indocyanine green as an index of hepatic blood flow and/or hepatic drug extraction has been tested and no significant effects have been found.

4.6 Pregnancy and lactation

Pregnancy: 'Pepcid' is not recommended for use in pregnancy, and should be prescribed only if clearly needed. Before a decision is made to use 'Pepcid' during pregnancy, the physician should weigh the potential benefits from the drug against the possible risks involved.
Although there is no experience with 'Pepcid' in human pregnancy, animal studies have shown that famotidine crosses the placental barrier without teratogenic effect, but some delay in maturation was seen in animals at high doses.

Breast feeding mothers: 'Pepcid' is secreted in human milk, therefore breast feeding mothers should either stop breast-feeding or stop taking the drug.

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable effects

In controlled studies, 'Pepcid' has been shown to be generally well tolerated.
Headache, dizziness, constipation, and diarrhoea have been reported rarely. Other side effects reported even less frequently included dry mouth, nausea and/or vomiting, abdominal discomfort or distension, anorexia, fatigue, rash, pruritus and urticaria, liver enzyme abnormalities, cholestatic jaundice, anaphylaxis, angioedema, arthralgia, muscle cramps, taste disorder, reversible psychic disturbances including depression, anxiety disorders, agitation, confusion, hallucinations, thrombocytopenia, leukopenia, and neutropenia. Interstitial pneumonia and Stevens Johnson syndrome/toxic epidermal necrolysis. have been reported very rarely. Convulsions, in patients with impaired renal function, have been reported very rarely. In addition to the above side effects, A-V block has been reported very rarely with H_2-receptor antagonists administered intravenously. Pancytopenia and leucopenia have been reported; however, a causal relationship to therapy with 'Pepcid' has not been established.

4.9 Overdose

The adverse reactions in overdose cases are similar to the adverse reactions encountered in normal clinical experience (see Section 4.8 Undesirable effects).. The usual measures to remove unabsorbed material from the gastro intestinal tract, clinical monitoring, and supportive therapy should be employed.
Patients with Zollinger-Ellison syndrome have tolerated doses up to 800 mg daily for more than a year without the development of significant adverse effects.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Mode of action: 'Pepcid' is a highly specific and potent competitive H_2 receptor antagonist. It has a rapid onset of action. Although the plasma half life of famotidine in patients is approximately 3.0 hours, 'Pepcid' has a long duration of action, and a single 40 mg dose has been shown to reduce gastric acid secretion for at least 10 hours.
'Pepcid' reduces the acid and pepsin content, as well as the volume of basal, nocturnal and stimulated gastric secretion.

In clinical studies, a single dose of 'Pepcid' at night relieved the pain associated with peptic ulcer, usually within a week, and suppressed gastric secretion.

5.2 Pharmacokinetic properties

'Pepcid' is a chemically novel competitive H_2 receptor antagonist with a guanidinothiazole ring. 'Pepcid' is rapidly absorbed, with dose related peak plasma concentrations reached in one to three hours. When used as recommended, there was no accumulation effect with repeated doses.
Protein binding in the plasma is relatively low (15-20%). The plasma half-life after a single oral dose or multiple repeated doses (for 5 days) was approximately 3 hours.
Metabolism of the drug occurs in the liver, with formation of the inactive sulphoxide metabolite.
Approximately 25-30% of the oral dosage is excreted in the urine, mainly as unchanged drug. A small amount may be excreted as the sulphoxide.

5.3 Preclinical safety data

Studies in animals and human volunteers have not shown anti-androgenic effects.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Carnauba Wax (E903)
Magnesium Stearate (E572)
Microcrystalline Cellulose (E460)
Pregelatinised Starch
Hydroxypropylcellulose (E463)
Hypromellose (E464)
Talc
Red Iron Oxide (E172)
Titanium Dioxide (E171)
Yellow Iron Oxide (E172)

6.2 Incompatibilities

Not applicable

6.3 Shelf Life

The shelf-life expiry date of this product shall be the date shown on the container and outer package of the product on the market in the country of origin.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

Opacified PVC-aluminium blister calendar packs of 28 tablets.

6.6 Special precautions for disposal and other handling

No special requirements.

7 Parallel Product Authorisation Holder

B&S Healthcare
Unit 4, Bradfield Road
Ruislip
Middlesex
HA4 0NU

8 Parallel Product Authorisation Number

PPA1328/117/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of First Authorisation: 12th June 2009

10 DATE OF REVISION OF THE TEXT